

**UkrAm Study of Thyroid Cancer and Other Thyroid Diseases in Ukraine  
Following the Chornobyl Accident**

Progress Report for Quarter Beginning 1 March and Ending 15 May, 2000

Project Manager

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For the reported period, the main efforts of the Project staff were directed towards intensification of the screening examination of cohort members. With this purpose, search of selection 1 cohort members was continued, using the following information sources:

- Passport Office and manual search in the town of Slavutych;
- Education Department and Tax Inspection of Zhytomyr oblast;
- Passport Office and Tax Inspection of Chernihiv oblast.

As a result of this search, the exact addresses of 1185 cohort members have been established.

During the reported period, search of persons residing in Kyiv oblast who had not responded to the invitation, has been performed. In January 2000, invitation letters have been sent out to 1218 potential cohort members who had been relocated from Polisia and Chornobyl raions and town of Prypyat to other raions of Kyiv oblast, to which 675 persons (55,4 %) have not answered. Lists of these persons have been transmitted to the medical staff of the raions in question in order to find out the addresses of these subjects, out of which 224 have been found.

During the quarter, 1940 invitations to take part in screening have been sent out to selection 2 cohort members. Search of these persons with the help of the medical staff of the raions under control has been started as well.

As a result of the work performed, from March 1, 2000 to May 15, 2000, 1927 cohort members have undergone primary medical screening examination, including 1359 persons from selection 1 and 588 persons from selection 2. 47 screening subjects (35 from selection 1 and 12 from selection 2) have been referred to fine needle aspiration biopsy (FNA) for thyroid nodules revealed in the process of screening. 29 FNAs have been performed in 26 patients (the rest of patients have not come to examination within the reported period). According to FNA data, a papillary carcinoma was suspected in one patient, confirmed later by postoperative pathohistological conclusion. In two patients adenomas of microfollicular structure have been diagnosed, and they have been operated. In one (female) patient an Ashkinasi's cell tumor has been identified according to FNA data.

For the reported period, 1540 final medical conclusions have been transmitted to raions under control in order to be delivered to screening subjects.

Because of lack of reagents for thyroid hormone and calcium determination within the March 2000, assay of their blood level has been started only from April 11, 2000.  $Ca^{++}$  level was determined in 1797 persons; TSH level in 683 patients; antiTPO in 683 subjects; Tg level in 683 patients.

During the reported period, selection 2 of cohort members has been finally approved and established to a volume of 14 000 records from the initial 75000-dose file. Databases and programmes for input of Cytologic conclusion form and Hospitalization form have been developed. A system of quality control of data input from Final medical conclusion forms has been worked out.

Changes have been made in the structure of the database of the Data Coordination Center

the University of Illinois. The first 200 sets of processed forms and electronic data have been received from this Center.

Data input from 437 Final medical conclusion forms was being performed.

For the reported period, 2400 complete sets of forms (Screening questionnaires, Blood examination, Final medical conclusions) have been prepared and transmitted to the Data Processing Center of the University of Illinois.

The visit of the ACERER Committee members has been organized. On April 14-15, 2000, meetings with participation of ACERER representatives have been held, devoted to progress in Project implementation. On April 3, 2000 a meeting (on the spot) dealing with Project implementation has been held with the medical authorities of Chernihiv oblast, as well as Ripky, Kozelets, and Chernihiv raions of Kyiv oblast.

## **II. Report on Tasks**

### **1. Establish and implement a management plan and quality control procedures for the study**

#### **1.4 Develop and implement quality control procedures for the study**

- In the framework of the working plan for quality control of the Project "Regulations on operation quality control for the Ukrainian-US Project members" have been developed, which state the main directions of quality control of the investigations being performed, errors are analysed, as well as the ways of their correcting.
- Instructions for Form completion on different stages of medical team activities have been revised; attention is paid to the correctness of filling in those Form items which contain information on quality control of medical data; a special attention is paid to the most typical cases of errors of Form completion.
- Meetings have been held with Project staff devoted to individual fields of work: with physicians-endocrinologists and ultrasonographers, with registrars, laboratory assistants (once a month). Meetings are held under the guidance of Prof. V.A. Oliynyk, Project Deputy Director for Clinical issues, and Prof. O.V. Epshtein, Head of the Central Laboratory.
- On an individual basis, in the process of work of teams control is performed of the work of the registrar, technician to USI-devices using a phantom; of conditions of storage and transportation of serum and urine; filling in the registration logs, Forms. Together with the team leader and team members, an analysis of quality control of the works performed is being made.
- At the Central Laboratory quality control of hormonal assays is being performed by comparing on Jacobson diagram the uniformity of the results of standards for each lot of kits. As a whole, hormonal kits supplied from Germany (Firm "Brahms") have a high reliability.
- Logistic support of the Laboratory is under strict control of the Project Director. Orders for purchase of up-to-date laboratory equipment are fulfilled according to the schedule of

temperature chart is plotted (A. Zaichenko is the responsible person); metrological control of centrifuge devices is carried out by engineer department staff; control of weighing, volumetric, biochemical equipment - by specialists in the corresponding field. Precision of micropipettes is verified by a weighing method under laboratory conditions (V.V. Markov).

- A considerable part of quality control covers checking of Form completion by team members before data input into computer DB. In the field the first control is performed by the team leader-endocrinologist, the second one in the process of establishing the final conclusion after receiving the results from the Laboratory. Before computer input, a selective control (1:10) is performed, or entire file control in case of pathology revealed (this work is being performed with V.A. Oliynyk). On the stage of computer input, questions arise concerning illegibility of medical terminology, bad hand, blanks in filling in the Forms.

## 2. Select a sample of records from the dose files to establish study cohort

### 2.3 Select the sample

Selection 2 sample has been finally approved and established to a size of 14000 records out of the initial 75000-dose file. Distribution of records is shown by the Tables below.

**Table 1. Distribution of records by dose and raions**

Raion	Number of records in 75000-file				Number of records left in the initial file after Selection 1 (55000-file)				
	A	B	C	Total	A	B	C	Total	% from 75000-cohort
Ivankiv	2847	608	237	3692	2521	434	0	2955	80
Chornobyl	2303	1264	876	4443	2034	925	0	2959	67
Polisya	2215	1142	850	4207	1964	844	0	2808	67
Town of Prypyat'	2066	1249	1015	4330	1845	901	0	2746	63
Narodychi	1455	2482	3457	7394	1298	1817	0	3115	42
Ovruch	7802	4182	1144	13128	6992	3064	0	10056	77
Ripky	5532	1564	398	7494	4950	1167	0	6117	82
Kozelets	7216	2240	718	10174	6420	1665	0	8085	79
Chernihiv	7903	2935	1257	12095	7059	2178	0	9237	76
City of Chernihiv	7194	1075	123	8392	6413	787	0	7200	86
<b>TOTAL</b>	<b>46533</b>	<b>18741</b>	<b>10075</b>	<b>75349</b>	<b>41496</b>	<b>13782</b>	<b>0</b>	<b>55278</b>	<b>73</b>

Year of birth	High dose		Middle dose			Low dose			All dose groups		
	M	F	M	F	not def	M	F	not def	M	F	not def
not defined	0	0	42	30	16	31	49	19	73	79	35
1982-86 (0-4)	0	0	396	424	180	566	603	380	962	1027	560
1976-81 (5-10)	0	0	548	492	199	1484	1509	734	2032	2001	933
1972-75 (11-14)	0	0	385	350	112	1432	1531	584	1817	1881	696
1968-71 (15-18)	0	0	168	135	40	573	719	290	741	854	330
Sum	0	0	1539	1431	547	4086	4411	2007	5625	5842	2554
Total	0		3517			10504			14021		

**Distribution of Selection 2 14000 cohort members by raions and dose group**

Raion	A	B	Total
Ivankiv	653	107	760
Chornobyl	507	242	749
Polisya	465	216	681
Town of Prypiat'	449	217	666
Narodychi	326	465	791
Ovruch	1736	803	2539
Ripky	1291	288	1579
Kozelets	1642	435	2077
Chernihiv	1815	529	2344
City of Chernihiv	1620	215	1835
Total	10504	3517	14021

### 3.3 Trace subjects for current address

In the current quarter information on current address of cohort from the following data sources has been obtained:

Name of the data source used (Selection 1)	Number of cohort members attempted to locate through this information source	Current address established within 3 study oblast	Live in Ukraine (outside of the catchment area)	Immigrated	Temporarily absent	Died	Not found	Double records
Slavutich city Passport Bureau	184	92	-	-	-	1	88	3
Department of Education of Zhitomyr Oblast State Administration.	572	123	-	2	-	-	447	-
State Taxation Administration of Zhitomyr Oblast State Administration	1364	213	-	-	-	-	1150	1
Cherhihiv Oblast Passport Bureau	1173	401	3	1	1	2	761	3
State Taxation Administration of Chernihiv oblast	2182	204	-	-	-	-	1978	-
Manual search by local medical staff in the Slavutich city.	168	148	-	1	3	-	16	-

Address search of the Selection 2 cohort members has started in the current quarter with the help of local medical staff in Narodichi and Ovruch raions of Zhitomyr oblast, Kozelets, Chernihiv, Ripki raions and Chernihiv city of Chernihiv oblast, Ivankiv raion of Kyiv oblast.

Tracing of Selection 2 cohort members is been done by Chernihiv oblast passport bureau.

In the current quarter clarification of addresses of some cohort members who did not respond to the mailing invitation has been performed.

In 1999 in Kyiv oblast (Ivankiv rayon is not included), 1218 persons, resettled from Chernobyl, Polissky raions and city Pripjat of Kyiv oblast were found using Kyiv oblast passport bureau and Chernobyl Department of Kyiv oblast. In January 2000 all of them were sent letters of invitation.

675 persons (55,4%) didn't respond to the letters of invitation, 64 letters (5%) returned to the Institute due to the wrong address. Lists of cohort members living within oblast according to our knowledge, were given to local medical staff for clarification of those addresses. Local medical staff made changes in the address and status information for 224 cohort members who didn't respond to the invitation.

In January 2000 were sent also 498 Invitation to the cohort members supposedly living in Ivankiv rayon of Kyiv oblast. We have not received back answers on 346 (70%) invitations. Local medical staff after additional work has made changes in the status and address information of 61 cohort members who didn't respond to our invitation.

#### **4. Enroll and maintain participation of subjects in the study**

##### **4.2 Send out initial invitation with information brochure**

Initial invitations for cohort members with information brochure were sent:

Narodichi rayon , Zhitomyr oblast – 200 invitations

Ovruch raion, Zhitomyr oblast – 900 invitations

Chernihiv city, Cherhihiv oblast – 50 invitations

Kozelets raion, Cherhihiv oblast - 500 invitations

Ripki raion, Cherhihiv oblast – 170 invitations

Also were sent 90 invitations to Selection 2 cohort members, which were resettled to the Slavutich city of Kyiv oblast and were not invited earlier.

## 5.5 Conduct screening examinations

From March 1 to May 15, 2000 primary examination was being performed (1359 patients - Selection 1; 568 patients - Selection 2). A total of 47 patients (35 from Selection 1 and 12 patients from Selection 2) have been referred to FNA of thyroid nodules.

29 FNAs have been performed to 26 patients (the rest of the patients have not turned up at the Institute's Clinic for second examination). According to FNA results, in one patient (male) a papillary carcinoma has been suspected (patient N.N. born in 1974).

The diagnosis has been confirmed during the operation. In two patients changes in nodular tissue corresponded to adenomas with microfollicular structure (patients I.D. born in 1985 and S.S. born in 1974). These patients have been operated on. In one patient (female) (B. born in 1974) cytological changes in the nodule corresponded to an Ashkinasi cell tumor. This patient has been hospitalized on May 26, 2000 for surgery. In the process of screening one patient (female) with 3 d. diffuse toxic goiter has been revealed. This patient had a compensated thyrotoxicosis. She has been operated on.

## 5.6 Notify subjects of final screening results

In the reported period local medical staff of study raions received for further distribution final medical conclusions and study results in following amounts:

	<b>Raions</b>	<b>Number of final medical conclusions sent</b>
1	Narodichi rayon	80
2	Ovruch raion	162
3	Ivankiv raion	40
4	Kozelets raion	395
5	Ripki raion	376
6	Chernihiv raion	549
7	Chernihiv city	283
	<b>Total</b>	<b>1885</b>



## **diseases**

### **7.1 Develop criteria for FNA**

Criteria for FNA performance have been agreed with the American Party.

### **7.2 Conduct FNA on appropriate subjects and refer appropriate subjects for surgery**

29 FNAs have been performed to 26 patients (28 FNAs in Selection 1 and one FNA in Selection 2). Based on the results of cytological study, 3 patients have been operated on (one case of suspicion of papillary carcinoma; two cases of adenomas with microfollicular structure).

### **7.3 Provide final diagnosis after surgery**

For the reported period, 4 patients have been operated following screening examinations (Table 7).

In one male aged 26 years (ID 01005309, exposure dose 0.06 Gy, group "A") a papillary carcinoma with dominant follicular structure (diameter 13 mm) has been diagnosed both by intraoperative and postoperative pathomorphologic analysis

In one male aged 26 years (ID 00063918, exposure dose 0.3 Gy, group "B") a normomicrofollicular adenomatous nodular goiter (diameter 15 mm) has been diagnosed both by intraoperative and postoperative pathomorphologic analysis.

In one boy aged 14 years (ID 09331117, exposure dose 28.2 Gy, group "C") a multinodular goiter of microfollicular-solid structure with oxyphilic-cell changes has been diagnosed both by intraoperative and postoperative pathomorphologic analysis. 7 nodules measuring 2 to 7 mm in diameter have been identified in both thyroid lobes.

In one female aged 26 years (ID 06972226, exposure dose 0.3 Gy, group "B") a diffuse toxic goiter (Graves' disease) with dominant microfollicular structure with signs of chronic thyroiditis weighing 46 g has been diagnosed both by intraoperative and postoperative pathomorphologic analysis.

Histological processing of biopsy material has been performed. Additional histological specimens have been prepared from paraffin blocks of the tumor removed and extratumoral tissue for the morphologic data bank of the Ukraine-US Project, and for additional verification by the international Panel of experts-pathologists. Appropriate Pathology Forms have been filled in.

Besides, in order to provide to epidemiologists additional information on cohort members concerning the possibility of surgical treatment for thyroid pathology before invitation to screening, collection of data and biopsy material has been continued from patients born in 1968 and later, who are living in regions under screening and have been operated during the reported period. Among 53 such cases an adolescent aged 16 years (ID 08504926, exposure dose 5.8 Gy, group "C") has been identified as a possible cohort member (Selection 1) with a partially encapsulated papillary carcinoma of papillary-solid structure, who is dwelling now in Kyiv oblast (in the cohort -

epidemiologists for final identification.

#### **7.4 Develop criteria for follow-up of subjects with other abnormal findings**

The following patients are liable to endocrinological follow-up:

- patients with autoimmune thyroiditis (also the subjects with a revealed increase in ATPO level);
- patients with hypothyroidism (laboratory and overt forms);
- patients with diffuse toxic goiter;
- patients with the diagnosis of “nodular goiter” (diagnosis confirmed by cytological study of FNA material);
- patients with hypo- and hypercalcemia;
- patients operated on for benign and malignant thyroid tumors;
- patients with thyroiditis (acute, subacute, and chronic forms).

#### **7.5 Complete laboratory tests for subjects examined**

Determination of TSH, Anti-TPO, Tg blood levels has been started from April 11, 2000 due to lack of reagents.

Ca<sup>++</sup> level has been studied in 1797 persons. No deviations from the normal range have been found. TSH level has been determined in 683 persons. TSH level was unchanged in 614 persons (90 %), decreased in 2 (0.3 %), and increased in 67 persons (9.7 %). Anti-TPO level was normal in 620 out of 683 persons (90.8 %), increased in 53 persons (8.8 %). Tg blood level was unchanged in 654 persons (95.8 %), increased in 13 (1.9 %), and decreased in 16 persons (2.3%).

#### **7.6 Complete final endocrine summary for each subject**

Based on the results of laboratory examinations, 428 Final Endocrinological Conclusions have been completed.

#### **7.9 Conduct expert reviews of thyroid pathology for subjects who had surgery**

Histological preparations from 6 cases of papillary carcinoma and 3 cases of benign thyroid pathology, determined at previous stages, have been presented at the regular meeting of the international Panel of experts-pathologists (Cambridge, March 4-5, 2000) for additional verification. All diagnoses have been confirmed.

The above 4 cases of surgical thyroid pathology identified for the reported period, will be presented to the expert Panel in October 2000.

## **study**

### **8.1 To develop a computer DB for data storage**

A database and programme for input of Cytologic Conclusion Form has been developed. The database has been worked out taking into account the input of any number of punctured neoplasms for one cohort member. Database structure has been included in the corresponding chapter of the Data Coding Manual.

A database and programme for input of Hospitalization Form have been worked out.

A system of quality control of data input from Final Conclusion Forms has been developed.

A programme for calculating the number of pathology revealed based on data from Final Endocrinological Conclusion Form (general summary Table, and pathology revealed for a concrete raion under study) has been developed. The possibility of printing a list of patients with a revealed concrete disease for a study raion is envisaged.

### **8.2 To develop a Data Coding and Documenting Manual.**

Changes have been made in database structure for compatibility with the database of the Data Processing Center of the University of Illinois (Institute of Pediatrics, Obstetrics and Gynecology). Programme convertors have been written. All changes have been documented and included in the Data Coding Manual. The first set (Ä0Ä0) out of 200 sets of processed forms and electronic data has been received from the University of Illinois (Institute of Pediatrics, Obstetrics and Gynecology).

### **8.3 To enter information from Data Collection Forms into the database**

Data input has been performed from Final Conclusion Forms containing pathology. For the reported period, data have been entered from 437 Final Conclusion Forms containing any thyroid pathology.

Data input from Fine Needle Biopsy Forms was being performed. Data input from Cytologic Conclusion Form has been started.

According to the schedule, complete sets of Forms (Screening questionnaires, Blood Examination, Final Conclusion Forms) have been prepared and transmitted to the Data Processing Center of the University of Illinois (Institute of Pediatrics, Obstetrics and Gynecology) in the following quantities:

Date of transmission	Quantity
03.04.2000	600
17.04.2000	600
05.05.2000	600
19.05.2000	300
24.05.2000	300
Total	2400

study subject is packed up in an individual envelope, marked and registered in the database.

## **9. Calculate estimate of dose and uncertainty for each study subject**

### **9.1 Determine the appropriate methods for calculating I-131 dose**

#### **9.1.1. Develop and field test dosimetry questionnaire.**

Version of the uniform Dosimetry Questionnaire (long form administration by dosimetrist ) and Self-administered Questionnaire (Short form, which is planned to be distributed with invitation letters) have been worked out and agreed with the Byelorussians. The first batch of Self-administered Questionnaires (5000 pcs.) has been printed in print shop and handed over to the epidemiologists to be dispatched together with invitation letters for subjects from Selection 2.

#### **9.1.2. Derive the thyroid dose rates from the direct thyroid measurements.**

There has been elaborated a dosimetric model to derive the thyroid dose rates and its uncertainties from the result of direct measurements on the thyroid level only. The model includes inputs of  $^{137}\text{Cs}$ ,  $^{134}\text{Cs}$  and  $^{136}\text{Cs}$  , as well as body surface contamination, into calculation of the signal measured on the thyroid with non-collimator-bearing SRP-68-01. The model has been implemented on the computer. There has been compiled a report describing the model to be presented at the joint dosimetric meeting in Minsk on May 31 - June 2, 2000.

#### **9.1.9. Analyze the responses provided by the interviewees (completeness, reliability, statistical distributions , etc.).**

9385 dosimetry questionnaires collected in 1992 and 3567 questionnaires collected during the 1998-2000 screening in Chernihiv oblast (334 questionnaires were provided by the same interviewees) have been computer-linked. Besides, 10073 questionnaires of Pripyat residents collected in 1988-1989 and 520 questionnaires of Pripyat residents collected during the screening in 1998-2000 (132 questionnaires were provided by the same interviewees) have also been computer-linked. The results of comparing responses on behavior pattern and intake of milk and stable iodine back in the earlier period following the accident and at this point of time have been put together in form of the presentation to be delivered at the joint dosimetric meeting in Minsk city.

The form of questionnaires in 1988-1992 was substantially different from the form of 1998-2000 questionnaires. Besides, surveys had different objectives in these two periods. This has hampered comparison of the information. We think it is necessary to re-interview a random sample of subjects during re-screening in certain time and to continue comparing the information being submitted.

In April 2000 on invitation of Professor I.A. Likhtarev, Mr. G.L. Moroz - who headed in 1986 a Group of specialists having organized performance of thyromonitoring in the territory of Ukraine - has been working in the Department of Dosimetry and Radiation Hygiene of the Research Center for Radiation Medicine (RCRM) of Ukraine. A list of questions has been preliminarily drawn up, concerning those thyroid activity measurements which are considered as problematic ones. These questions have been examined during a week of joint work with Mr. G.L. Moroz. Besides, Mr. G.L. Moroz has reported those organizational and technical details of the thyromonitoring performed in the territory of Ukraine in 1986, which he remembered.

In order to search persons who had been involved in thyromonitoring in the territory of Chernihiv oblast, and to collect technical documentation for devices having been used in thyromonitoring, several travels have been organized for a collaborator of RCRM to the town of Chernihiv (2 travels), settlements Ripky and Kozelets. Meetings have been organized with persons who have been working in 1986 in Chernihiv Oblast Department of Health or were senior officials of medical institutions, and have been dealing with organization of thyroid activity measurements in the territory of Chernihiv oblast. Meetings with members of the staff of medical institutions who personally performed measurements, have been organized as well. Moreover, persons have been questioned, who were responsible for the preparatory work: check of devices before measurements, organization of transportation of children in view of measurements, etc.

In Chernihiv Oblast Hospital technical documentation for the energoselective device NK-150, being missing before, as well as drawings of detector unit and collimator for the device GTRM-01c, have been found and copied (both devices were used for thyromonitoring).

We failed to meet those persons who have made measurements in the territory of the oblast using non-energoselective devices SRP-68-01. As followed from conversations with eye-witnesses (staff of medical institutions and sanitary epidemiologic station of settlements Ripky and Kozelets), these measurements had been made by groups having come from other oblasts. Local staff was used only for ancillary work (to ensure attendance of children in view of measurements). Taking into account that in the territory of Chernihiv oblast more than 30 % of all thyroid measurements have been made using SRP-68-01 devices, we consider it necessary to continue searching those persons who made these measurements.

#### **9.1.11. Estimate thyroid dose from I-131, as well as uncertainty, for each study subject.**

Doses and uncertainties have been calculated for 5 hypothetical subjects with intricate behavior patterns based on scenarios that were worked out by the American colleagues. There has been prepared description of the calculation method, written a program for computer implementation of the method, and compiled a presentation of the calculation method to be presented at the joint dosimetric meeting in Minsk.

Screening performance remains the main direction in the work for the two next quarters. Until the end of 2000, it is planned to complete formation of the 12000-cohort of Project participants who have undergone primary medical screening. In order to achieve this task, the following work is being planned for the two quarters:

1. To complete location and identification of potential cohort members of selection 1 who changed their place of residence as of April 26, 1986, and were relocated to other raions of oblasts being under control according to the Project protocol (Kyiv, Zhytomyr, Chernihiv oblasts).
2. To perform screening medical examination of those potential cohort members of selection 1 who have not yet undergone it.
3. To continue and complete location and identification of potential cohort members of selection 2.
4. To perform screening medical examination of potential cohort members of selection 2.
5. To perform input of screening results into the Project database.
6. To settle the matter of performing a timely thorough medical examination on the basis of the Clinic of the Institute of Endocrinology and Metabolism of the AMS of Ukraine for those cohort members in which thyroid pathology was suspected in the process of primary screening (organization measures, payment of their fares for reaching the screening center).
7. To carry out preparatory work in view of second screening of cohort members:
  - to make changes in screening examination forms;
  - to develop the procedure of invitation to the second screening.
  - to prepare an information leaflet-invitation for cohort members;
  - to perform a reattestation of the Project executive staff members who are directly involved in screening performance, are responsible for laboratory investigations and for processing of the results of medical screening examination.
8. To prepare a joint meeting of Belarus, American and Ukraine executors of the Project, dealing with clinical issues of Project implementation.
9. To prepare a meeting of Project Review Boards on September 23-24, 2000.
10. To prepare a meeting devoted to the issues of Project implementation in Washington (November 13-17, 2000).
11. To prepare materials for publication concerning the organization and statistical force of screening examination of Project subjects, and on the results of medical examination of the first 4000 cohort members.